REMARKS

Applicants respectfully request reconsideration of the pending claims in view of the above amendments and the following remarks. Claims 24-27, 35-37, 60-63, and 65-99 have been canceled. Claims 45-59 and 64 have been amended. Claims 100-104 have been added. Claims 45-59, 64, and 100-104 are currently pending.

No new matter has been inserted. Support for the limitation of a composition in claims 45-59 and 64 can be found in the specification at p. 3, line 29; p. 4, lines 1-7; p. 4, line 27; and throughout the specification. Support for the limitation of a carrier in claims 45-59 and 64 can be found in the specification at p. 21, lines 12-21. Claims 46, 48, 50-53, 55-56, 58, and 64 have also been amended to put them in independent form. Claim 100 has support in claim 59, in the specification at p. 6, lines 18-20, and with respect to percent identity at p. 7, line 32 and p. 8, line 29. Claim 101 has support in claim 57. Claim 102 has support in claim 58. Claim 103 has support in claim 49. Claim 104 has support in claim 50.

35 U.S.C. § 112, first paragraph

Claims 24-27, 35-37 and 45-99 were rejected under 35 U.S.C. § 112, first paragraph, for written description. Applicants respectfully traverse this rejection.

The Examiner alleges that the written description is not commensurate in scope with the claims but does allow that the specification teaches specific amino acid substitutions at amino acid positions 12, 15, 17, 35, and 38 of SEQ ID NO: 2. While not conceding the correctness of Examiner's position, in the interest of advancing prosecution, Applicants have amended the claims to include specific amino acid substitutions at amino acid positions 12, 15, 17, 35, or 38 of SEQ ID NO: 2.

Further, the claims reciting "97.5% identity" have been canceled. The remaining claims are directed to SPE-C toxins that are fully supported by an adequate written description. The remaining claims recite specific amino acid substitution locations that have been exemplified in the specification including amino acid positions 12, 15, 17, 35, and 38 of SEQ ID NO: 2.

Specifically, aspartic acid-12 of SEQ ID NO: 2 is exemplified in the specification at page 39. Similarly, tyrosine-15 of SEQ ID NO: 2 is exemplified at pages 36-39. Tyrosine-17 of SEQ

ID NO: 2 is exemplified at pages 36-39. Histidine-35 of SEQ ID NO: 2 is exemplified at page 39. Asparagine-38 of SEQ ID NO: 2 is exemplified at pages 36-39. As all of the substitution locations in the pending claims are exemplified in the specification, one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). Therefore, Applicants respectfully request that this rejection be withdrawn.

To the extent that this rejection is applied to new claims 100-104, the following comments are provided. Claims 100-104 recite specific amino acid substitution locations that have been exemplified in the specification including amino acid positions 12, 15, 17, 35, and 38 of SEQ ID NO: 2. Claims 100 now recites the limitation "99% identical to SEQ ID NO: 2." Applicants submit that this limitation is adequately supported such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Specifically, Applicants describe this degree of identity at both p. 7, line 32 and at p. 8, line 29. Applicants point out that SEQ ID NO: 2 is 235 amino acids in length, accordingly 99% translates to 2 or 3 amino acid changes depending on whether the number is rounded up or down. In view of this, Applicants submit that they have provided sufficient disclosure so as to properly demonstrate to one of skill in the art that they possessed "An isolated Streptococcal pyrogenic exotoxin type C comprising an amino acid substitution at aspartic acid-12 of SEQ ID NO: 2, at tyrosine-15 of SEQ ID NO: 2, at tyrosine-17 of SEQ ID NO: 2, at histidine-35 of SEQ ID NO: 2, or at asparagine-38 of SEQ ID NO: 2, wherein the isolated Streptococcal pyrogenic exotoxin type C is 99% identical to SEQ ID NO: 2, wherein the isolated Streptococcal pyrogenic exotoxin type C has reduced toxicity compared with wild-type" as required by claim 100.

Applicants further direct the attention of the Examiner to the information provided by Brian R. Stanton, a Quality Assurance Specialist for Technology Center 1600, at the Biotechnology/Chemistry/Pharmaceutical Customer Partnership meeting held on July 29, 2002. (A courtesy copy of the slides from this presentation is attached hereto.) In this commentary, Mr. Stanton provides that with regard to what % homology is appropriate, having demonstration of an activity, and having a limitation in the claims regarding that activity, may be helpful in

resolving whether or not a particular % of homology is appropriate. In the present case, the activity of "reduced toxicity compared with wild-type" is present in claim 100.

Further, Mr. Stanton provides that information regarding critical residues and possible residue variations is also to be considered when determining whether a particular % of homology is appropriate. In this case, the specification is replete with information on particular residues of interest and possible variations including substitutions. As previously argued, p. 11, line 7 through p. 17, line 5 is almost entirely devoted to structural regions of interest and specific residues of interest. For example, the specification discusses a mutant comprising an amino acid substitution in a β-barrel of a B-subunit or a N-terminal alpha helix. At least page 11, lines 12 - 22 of the specification supports mutations on β-barrel 4 of B-subunit 5. Particular amino acids supported as points for mutation in the β-barrels include His-35, Asn-38, Thr-33 and Leu-36. At least page 13, lines 16 - 24 of the specification supports mutations on N-terminal alpha helix 51. Particular amino acids supported as points for mutation in the N-terminal alpha helix include Ser-11, Asp-12, Tyr-15 and Tyr-17. At least page 13, line 25 through page 14, line 5 supports mutations on a central alpha helix. Particular amino acids supported as points for mutation in the central alpha helix include Lys-135, Lys-138, Tyr-139, and Asp-142. Moreover, claim 100 actually recites specific residues and therefore meets the standards of Mr. Stanton's presentation.

For at least these reasons, Applicants submit that adequate written description has been provided. Applicants respectfully request that this rejection be withdrawn.

35 U.S.C. § 112, second paragraph

Claims 24-26, 35-37 and 59 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully traverse this rejection.

While not conceding in the correctness of the Examiner's position, in the interest of advancing prosecution, Applicants have canceled claims 24-26 and 35-37 to obviate this rejection. Applicants have further amended claim 59 to make it clear that "these amino acids" refers to the specified amino acids of SEQ ID NO: 2. Applicants respectfully request that this rejection be withdrawn.

Summary

Applicants assert that each of claims 45-59, 64, and 100-104 are in condition for allowance, and notification to that effect is earnestly solicited.

The Examiner is invited to contact Applicants' undersigned representative at the telephone number provided below, if the Examiner believes that doing so will expedite prosecution of the application.

Respectfully submitted,

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